LYC 1/26/03
STN - search
text.

(FILE 'HOME' ENTERED AT 19:06:30 ON 26 JAN 2003)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, CANCERLIT' ENTERED AT 19:07:03 ON 26 JAN 2003

L1	74052	S	SIMULTANEOUS AND DRUG
L2	0	S	L1 AND (CLOSE PROXIMATY)
L3	29	S	L1 AND (CLOSE PROXIMITY)
L4	21		DUPLICATE REMOVE L3 (8 DUPLICATES REMOVED)
L5	24503	S	(CLOSE PROXIMITY)
L6	2017	S	L5 AND DRUG
L7	0	S	L5 AND DRUG ANALOG
L8	1499	S	(DRUG ANALOG)
L9	0	S	L8 AND L6
L10	0	S	L8 AND L5
L11	52	S	L8 AND ANTIBOD?
L12	0	S	L11 AND SIGNAL
L13	8	S	L11 AND ENZYME?
L14	1767	S	L5 AND SIGNAL
L15	159	S	L14 AND DRUG
L16	27	S	L15 AND ANTIBOD?
L17	17		DUPLICATE REMOVE L16 (10 DUPLICATES REMOVED)

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L15	159	S	L14 AND DRUG
L16	27	S	L15 AND ANTIBOD?
L17	17		DUPLICATE REMOVE L16 (10 DUPLICATES REMOVED)

=>

17 ANSWER 12 OF 17 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 5
AN 1998:355950 BIOSIS
DN PREV199800355950
TI Development of a CD218/CD86 (B7-2) binding assay for high throughput screening by homogeneous time-resolved fluorescence.
AU Mellor, Geoffrey W. (1); Burden, M. Neil; Preaudat, Marc; Joseph, Yvonne; Cooksley, Susan B.; Ellis, Jonathan H.; Banks, Martyn N.
CS (1) Lead Discovery Unit, Glaxo Wellcome Res. Dev., Stevenage UK
SO Journal of Biomolecular Screening, (Summer, 1998) Vol. 3, No. 2, pp. 91-99.
ISSN: 1087-0571.
DT Article
LA English
AB CD28 has been demonstrated to provide the major costimulatory **signal** for CD4-positive T cells. Ligation with its natural ligands CD80 (B7-1) and CD86 (B7-2) leads to **signals** during activation that are required for the production of interleukin-2, and this process has been implicated in the regulation of T-cell anergy and programmed cell death. This article describes the assay development, assay validation, and primary screening for small molecule antagonists of this interaction, which could be potential **drug** candidates. The assay uses homogeneous time-resolved fluorescence based on energy transfer from excited europium ions to cross-linked allophycocyanin, which then subsequently emits a fluorescent **signal**. An "indirect" approach was taken, whereby the cross-linked allophycocyanin (XL665) is covalently linked to an antihuman **antibody** that binds to a human immunoglobulin (Ig) domain fused to CD28. The CD86 that is expressed as a fusion protein with a rat Ig domain is bound to biotinylated sheep antirat **antibody**, which is complexed with streptavidin-europium cryptate. This "cassette" format facilitates the development of related assays using CTLA-4 in place of CD28 and/or CD80 in place of CD86, allowing easy determination of the selectivity of active compounds. When the CD28 and CD86 are in **close proximity** (i.e., bound), there is a specific time-resolved emission at 665 nm that is largely absent in either unbound partner. Experiments to optimize the reagent concentrations, incubation time, solvent effects and quench effects by colored compounds are discussed, as are the results from robustness testing and data from primary screening.
CC Biochemical Methods - General *10050
Biochemical Studies - General *10060
Biophysics - General Biophysical Techniques *10504
IT Major Concepts
Biochemistry and Molecular Biophysics; Methods and Techniques
IT Chemicals & Biochemicals
anti-CD28 monoclonal **antibody**: Sigma; anti-CD86 monoclonal **antibody**: Pharmingen; europium cryptate-labeled streptavidin: CIS biointernational; sheep antirat IgG2b [sheep antirat immunoglobulin G2b]: The Binding Site; CD28; CD28/CD86 binding antagonists: analysis, high throughput screening; CD86 [B7-2]; XL665-labeled antihuman **antibody**: CIS biointernational
IT Methods & Equipment
homogeneous time-resolved fluorescence black 96-well plate: Wallac, laboratory equipment; homogeneous time-resolved fluorescence: Analysis/Characterization Techniques: CB, screening method; scintillation proximity assay: Analysis/Characterization Techniques: CB, analytical method; CD218/CD86 (B7-2) binding assay: activity assays, analytical method, development; Wallac 96-well microtiter plate: Wallac, laboratory equipment
RN 9013-20-1 (STREPTAVIDIN)

L17 ANSWER 13 OF 17 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 97349762 EMBASE

17 ANSWER 12 OF 17 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 5
AN 1998:355950 BIOSIS
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Biochemical Studies - General *10060
Biophysics - General Biophysical Techniques *10504
IT Major Concepts
Biochemistry and Molecular Biophysics; Methods and Techniques
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IT Methods & Equipment
homogeneous time-resolved fluorescence black 96-well plate: Wallac, laboratory equipment; homogeneous time-resolved fluorescence: Analysis/Characterization Techniques: CB, screening method; scintillation proximity assay: Analysis/Characterization Techniques: CB, analytical method; CD218/CD86 (B7-2) binding assay: activity assays, analytical method, development; Wallac 96-well microtiter plate: Wallac, laboratory equipment
RN 9013-20-1 (STREPTAVIDIN)

L17 ANSWER 13 OF 17 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 97349762 EMBASE

17 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 4
AN 2000:850623 CAPLUS
DN 135:13785
TI Development of a ubiquitin transfer assay for high throughput screening by fluorescence resonance energy transfer
AU Boisclair, Michael D.; McClure, Christopher; Josiah, Serene; Glass, Susan; Bottomley, Steve; Kamerkar, Shubi; Hemmila, Ilkka
CS GPC Biotech, Inc., Cambridge, MA, USA
SO Journal of Biomolecular Screening (2000), 5(5), 319-328
CODEN: JBISF3; ISSN: 1087-0571
PB Mary Ann Liebert, Inc.
DT Journal
LA English
CC 1-1 (Pharmacology)
AB An assay based on fluorescence resonance energy transfer (FRET) has been developed to screen for ubiquitination inhibitors. The assay measures the transfer of ubiquitin from Ubc4 to HECT protein Rsc 1083. Secondary reagents (streptavidin and **antibody** to glutathione-S-transferase [GST]), pre-labeled with fluorophores (europium chelate, Eu3+, and allophycocyanin [APC]), are noncovalently attached via tags (biotin and GST) to the reactants (ubiquitin and Rsc). When Rsc is ubiquitinated, Eu3+ and APC are brought into **close proximity**, permitting energy transfer between the two fluorescent labels. FRET was measured as time-resolved fluorescence at the emission wave-length of APC, almost entirely free of nonspecific fluorescence from Eu3+ and APC. The FRET assay generated a lower ratio of **signal** to background (8 vs. 31) than an assay for the same ubiquitination step that was developed as a dissocn.-enhanced lanthanide fluoroimmunoassay (DELFIA). However, compared to the DELFIA method, use of FRET resulted in higher precision (4% vs. 11% intraplate coeff. of variation). Quenching of fluorescence was minimal when compds. were screened at 10 .mu.g/mL using FRET. Employing a quick and simple homogeneous method, the FRET assay for ubiquitin transfer is ideally suited for high throughput screening.
ST ubiquitin transfer assay high throughput screening
IT Bioassay
(FRET; ubiquitin transfer assay for high throughput screening by fluorescence resonance energy transfer)
IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(HECT, Rsc 1083; ubiquitin transfer assay for high throughput screening by fluorescence resonance energy transfer)
IT Immunoassay
(fluorescence; ubiquitin transfer assay for high throughput screening by fluorescence resonance energy transfer)
IT **Drug** screening
(for ubiquitin inhibitors; ubiquitin transfer assay for high throughput screening by fluorescence resonance energy transfer)
IT Fluorometry
(ubiquitin transfer assay for high throughput screening by fluorescence resonance energy transfer)
IT 60267-61-0, Ubiquitin
RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(ubiquitin transfer assay for high throughput screening by fluorescence resonance energy transfer)
RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Earnshaw, D; J Biomol Screen 1999, V4, P239 CAPLUS
(2) Handley, P; Proc Natl Acad Sci USA 1991, V88, P258 CAPLUS
(3) Hemmila, I; Anal Biochem 1984, V137, P335 CAPLUS
(4) Hemmila, I; Drug Discov Today 1997, V2, P373 CAPLUS
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AN 2000:850623 CAPLUS
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CS GPC Biotech, Inc., Cambridge, MA, USA
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DT Journal
LA English
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ST ubiquitin transfer assay high throughput screening
IT Bioassay
(FRET; ubiquitin transfer assay for high throughput screening by fluorescence resonance energy transfer)
IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(HECT, Rsc 1083; ubiquitin transfer assay for high throughput screening by fluorescence resonance energy transfer)
IT Immunoassay
(fluorescence; ubiquitin transfer assay for high throughput screening by fluorescence resonance energy transfer)
IT **Drug** screening
(for ubiquitin inhibitors; ubiquitin transfer assay for high throughput screening by fluorescence resonance energy transfer)
IT Fluorometry
(ubiquitin transfer assay for high throughput screening by fluorescence resonance energy transfer)
IT 60267-61-0, Ubiquitin
RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)
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(3) Hemmila, I; Anal Biochem 1984, V137, P335 CAPLUS
(4) Hemmila, I; Drug Discov Today 1997, V2, P373 CAPLUS
(5) Hemmila, I; High Throughput Screening 1997, V2, P211

(6) Jentsch, S; Annu Rev Genet 1992, V26, P179 CAPLUS
(7) Jentsch, S; Cell 1995, V82, P881 CAPLUS
(8) Kolb, J; J Biomol Screen 1996, V1, P203 CAPLUS
(9) Mathis, G; Clin Chem 1993, V39, P1953 CAPLUS
(10) Mathis, G; Clin Chem 1995, V41, P1391 CAPLUS
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(23) Zhang, J; J Biomol Screen 1999, V4, P67

(6) Jentsch, S; Annu Rev Genet 1992, V26, P179 CAPLUS
(7) Jentsch, S; Cell 1995, V82, P881 CAPLUS
(8) Kolb, J; J Biomol Screen 1996, V1, P203 CAPLUS
(9) Mathis, G; Clin Chem 1993, V39, P1953 CAPLUS
(10) Mathis, G; Clin Chem 1995, V41, P1391 CAPLUS
(11) Mellor, G; J Biomol Screen 1998, V3, P91 CAPLUS
(12) Morrison, L; Anal Biochem 1988, V174, P101 CAPLUS
(13) Rolfe, M; J Mol Med 1997, V75, P5 CAPLUS
(14) Rolfe, M; Proc Natl Acad Sci USA 1995, V92, P3264 CAPLUS
(15) Scheffner, M; Cell 1993, V75, P495 CAPLUS
(16) Selvin, P; J Am Chem Soc 1994, V116, P6029 CAPLUS
(17) Selvin, P; Methods Enzymol 1995, V246, P300 CAPLUS
(18) Selvin, P; Proc Natl Acad Sci USA 1994, V91, P10024 CAPLUS
(19) Stenroos, K; Cytokine 1998, V10, P495 CAPLUS
(20) Szllosi, J; Cytometry 1998, V34, P159
(21) Van Der Meer, B; Resonance Energy Transfer: Theory and Data 1994
(22) Wu, P; Anal Biochem 1994, V218, P1 CAPLUS
(23) Zhang, J; J Biomol Screen 1999, V4, P67

L17 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2003 ACS
AN 1999:736359 CAPLUS
DN 131:334316
TI Method and apparatus for measuring binding between biological molecules
PA IA Inc., USA
SO Eur. Pat. Appl., 43 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM G01N021-77
CC 9-1 (Biochemical Methods)
Section cross-reference(s): 1, 2

✓ printed

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 957354	A2	19991117	EP 1999-302175	19990322
	EP 957354	A3	20000322		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	US 6251688	B1	20010626	US 1998-45223	19980320
	US 6300082	B1	20011009	US 1998-45224	19980320
	US 2001023077	A1	20010920	US 2001-833998	20010412
	US 2002137055	A1	20020926	US 2001-910628	20010720
PRAI	US 1998-45223	A	19980320		
	US 1998-45224	A	19980320		

AB A method and app. for measuring binding between a plurality of mols. of a first type and a plurality of mols. of a second type is presented. App. utilizes a sensor possessing a waveguide to which have been attached in **close proximity** to its surface, features resembling mols. of said first type. Light is injected into said waveguide so as to produce an evanescent field at its surface. Mols. of said second type are tagged with a tag belonging to that class of chems. which alters a characteristic of light when said light passes through said chem. tag. App. utilizes are rapid means of monitoring the change in optical **signal** coming from said waveguide as binding proceeds between tagged mols. of type 2 and the feature resembling mols. of type 1 on said waveguide. This allows direct measurement of binding and dissocn. rates between the two types of mols. Methods are provided whereby such data may be used to compute affinity consts., binding activity, complex affinity consts. resulting from cooperativity, and kinetic parameters for the mol. pair. Preferred embodiments of the invention illustrate application of the method and app. to measuring binding between biol. receptors and their nuclear response elements, and the use of this type of measurement for assessment of the activity of hormonal mimics present in a sample, for evaluation of pharmaceuticals intended to treat hormone dependent cancers, and for evaluation of tissue biopsy samples to detect mutant forms of the p53 protein.

ST app binding biol mol

IT Pipes and Tubes
(Cylindrical; method and app. for measuring binding between biol. mols.)

IT Genetic element
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process)
(ERE (estrogen-responsive element); method and app. for measuring binding between biol. mols.)

IT Solvents
(Perfluoroalkane; method and app. for measuring binding between biol. mols.)

IT Containers
(cartridges; method and app. for measuring binding between biol. mols.)

IT Neoplasm
(hormone dependent; method and app. for measuring binding between biol. mols.)

L17 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2003 ACS
AN 1999:736359 CAPLUS
DN 131:334316
TI Method and apparatus for measuring binding between biological molecules
PA IA Inc., USA
SO Eur. Pat. Appl., 43 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM G01N021-77
CC 9-1 (Biochemical Methods)
Section cross-reference(s): 1, 2
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 957354	A2	19991117	EP 1999-302175	19990322
	EP 957354	A3	20000322		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	US 6251688	B1	20010626	US 1998-45223	19980320
	US 6300082	B1	20011009	US 1998-45224	19980320
	US 2001023077	A1	20010920	US 2001-833998	20010412
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(Cylindrical; method and app. for measuring binding between biol. mols.)

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IT Solvents
(Perfluoroalkane; method and app. for measuring binding between biol. mols.)

IT Containers
(cartridges; method and app. for measuring binding between biol. mols.)

IT Neoplasm
(hormone dependent; method and app. for measuring binding between biol. mols.)

IT Affinity
Animal tissue
Apparatus
Biochemical molecules
Caps
Carriers
Dissociation kinetics
Drugs
Fluorescent substances
Light sources
Luminescent substances
Mutation
Optical fibers
Optical waveguides
Reaction kinetics
Semiconductor lasers
Sensors
Spectrometers
(method and app. for measuring binding between biol. mols.)

IT p53 (protein)
RL: ANT (Analyte); ANST (Analytical study)
(method and app. for measuring binding between biol. mols.)

IT **Antibodies**
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(method and app. for measuring binding between biol. mols.)

IT Androgens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(method and app. for measuring binding between biol. mols.)

IT Androgen receptors
Estrogen receptors
Estrogens
Hormone receptors
Progesterone receptors
Proteins, general, biological studies
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process)
(method and app. for measuring binding between biol. mols.)

IT Ligands
Nucleotides, biological studies
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)
(method and app. for measuring binding between biol. mols.)

IT Enzymes, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(method and app. for measuring binding between biol. mols.)

IT Glass, uses
RL: DEV (Device component use); USES (Uses)
(method and app. for measuring binding between biol. mols.)

IT Receptors
RL: RCT (Reactant); RACT (Reactant or reagent)
(method and app. for measuring binding between biol. mols.)

IT Hormones, animal, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(mimics; method and app. for measuring binding between biol. mols.)

IT 57-83-0, Progestin, biological studies 1852-49-9, Pregnanediol-3-glucuronide 2479-90-5, Estrone-3-glucuronide
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(method and app. for measuring binding between biol. mols.)

IT 37626-13-4 60676-86-0, Fused silica
RL: DEV (Device component use); USES (Uses)
(method and app. for measuring binding between biol. mols.)

IT Affinity
Animal tissue
Apparatus
Biochemical molecules
Caps
Carriers
Dissociation kinetics
Drugs
Fluorescent substances
Light sources
Luminescent substances
Mutation
Optical fibers
Optical waveguides
Reaction kinetics
Semiconductor lasers
Sensors
Spectrometers
(method and app. for measuring binding between biol. mols.)

IT p53 (protein)
RL: ANT (Analyte); ANST (Analytical study)
(method and app. for measuring binding between biol. mols.)

IT **Antibodies**
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(method and app. for measuring binding between biol. mols.)

IT Androgens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(method and app. for measuring binding between biol. mols.)

IT Androgen receptors
Estrogen receptors
Estrogens
Hormone receptors
Progesterone receptors
Proteins, general, biological studies
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process)
(method and app. for measuring binding between biol. mols.)

IT Ligands
Nucleotides, biological studies
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)
(method and app. for measuring binding between biol. mols.)

IT Enzymes, biological studies
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(method and app. for measuring binding between biol. mols.)

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RL: DEV (Device component use); USES (Uses)
(method and app. for measuring binding between biol. mols.)

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IT Hormones, animal, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(mimics; method and app. for measuring binding between biol. mols.)

IT 57-83-0, Progestin, biological studies 1852-49-9, Pregnanediol-3-glucuronide 2479-90-5, Estrone-3-glucuronide
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(method and app. for measuring binding between biol. mols.)

IT 37626-13-4 60676-86-0, Fused silica
RL: DEV (Device component use); USES (Uses)
(method and app. for measuring binding between biol. mols.)

L17 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2003 ACS
AN 2000:161447 CAPLUS
DN 132:204636
TI Human G protein-coupled receptor 14926, its cDNA sequence, and its diagnostic and therapeutic uses
IN Glucksmann, Maria Alexandra; Silos-santiago, Inmaculada
PA Millennium Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N015-12
ICS C07K014-705; C07K016-28; C12Q001-68; G01N033-53; G01N033-68; A61K038-16; A01K067-027
CC 6-3 (General Biochemistry)
Section cross-reference(s): 3, 13, 63
FAN.CNT 5

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000012707	A1	20000309	WO 1999-US20084	19990902
W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9958010	A1	20000321	AU 1999-58010	19990902
PRAI US 1998-145745	A	19980902		
US 1999-383745	A	19990826		
WO 1999-US20084	W	19990902		

AB The present invention relates to a newly identified receptor belonging to the superfamily of G-protein-coupled receptors. The receptor, designated 14926, has a **signal** transduction signature motif in its transmembrane domain, and exhibits homol. to serotonin receptor. The invention also relates to polynucleotides encoding the receptor, which maps to human chromosome 7 in **close proximity** to marker Bda06f04. The invention further relates to methods using the receptor polypeptides and polynucleotides as a target for diagnosis and treatment in receptor-mediated disorders. The invention further relates to **drug**-screening methods using the receptor polypeptides and polynucleotides to identify agonists and antagonists for diagnosis and treatment. The invention further encompasses agonists and antagonists based on the receptor polypeptides and polynucleotides. The invention further relates to procedures for producing the receptor polypeptides and polynucleotides.
ST G protein coupled receptor 14926 cDNA sequence human
IT G protein-coupled receptors
RL: BOC (Biological occurrence); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(14926; human G protein-coupled receptor 14926, its cDNA sequence, and its diagnostic and therapeutic uses)
IT cDNA sequences
(for human G protein-coupled receptor 14926)
IT Chromosome
(human 7, gene mapping to chromosome 7; .human G protein-coupled receptor 14926, its cDNA sequence, and its diagnostic and therapeutic uses)
IT **Drug** screening
Drugs

L17 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2003 ACS
AN 2000:161447 CAPLUS
DN 132:204636
TI Human G protein-coupled receptor 14926, its cDNA sequence, and its diagnostic and therapeutic uses
IN Glucksmann, Maria Alexandra; Silos-santiago, Inmaculada
PA Millennium Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N015-12
ICS C07K014-705; C07K016-28; C12Q001-68; G01N033-53; G01N033-68; A61K038-16; A01K067-027
CC 6-3 (General Biochemistry)
Section cross-reference(s): 3, 13, 63
FAN.CNT 5

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000012707	A1	20000309	WO 1999-US20084	19990902
W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9958010	A1	20000321	AU 1999-58010	19990902
PRAI US 1998-145745	A	19980902		
US 1999-383745	A	19990826		
WO 1999-US20084	W	19990902		

AB The present invention relates to a newly identified receptor belonging to the superfamily of G-protein-coupled receptors. The receptor, designated 14926, has a **signal** transduction signature motif in its transmembrane domain, and exhibits homol. to serotonin receptor. The invention also relates to polynucleotides encoding the receptor, which maps to human chromosome 7 in **close proximity** to marker Bda06f04. The invention further relates to methods using the receptor polypeptides and polynucleotides as a target for diagnosis and treatment in receptor-mediated disorders. The invention further relates to **drug**-screening methods using the receptor polypeptides and polynucleotides to identify agonists and antagonists for diagnosis and treatment. The invention further encompasses agonists and antagonists based on the receptor polypeptides and polynucleotides. The invention further relates to procedures for producing the receptor polypeptides and polynucleotides.
ST G protein coupled receptor 14926 cDNA sequence human
IT G protein-coupled receptors
RL: BOC (Biological occurrence); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(14926; human G protein-coupled receptor 14926, its cDNA sequence, and its diagnostic and therapeutic uses)
IT cDNA sequences
(for human G protein-coupled receptor 14926)
IT Chromosome
(human 7, gene mapping to chromosome 7; .human G protein-coupled receptor 14926, its cDNA sequence, and its diagnostic and therapeutic uses)
IT **Drug** screening
Drugs

Epitopes
Genetic mapping
Immunoassay
Molecular cloning
Nucleic acid hybridization
Test kits
(human G protein-coupled receptor 14926, its cDNA sequence, and its diagnostic and therapeutic uses)

IT **Antibodies**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(human G protein-coupled receptor 14926, its cDNA sequence, and its diagnostic and therapeutic uses)

IT Gene, animal
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(mapping to chromosome 7; human G protein-coupled receptor 14926, its cDNA sequence, and its diagnostic and therapeutic uses)

IT Brain
Heart
Hyperplasia
Inflammation
Kidney
Liver
Lung
Muscle
Spleen
(modulation of receptor activity in; human G protein-coupled receptor 14926, its cDNA sequence, and its diagnostic and therapeutic uses)

IT Protein sequences
(of human G protein-coupled receptor 14926)

IT Animal
(transgenic; human G protein-coupled receptor 14926, its cDNA sequence, and its diagnostic and therapeutic uses)

IT 243132-22-1DP, subfragments are claimed
RL: BOC (Biological occurrence); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(amino acid sequence; human G protein-coupled receptor 14926, its cDNA sequence, and its diagnostic and therapeutic uses)

IT 260239-96-1P
RL: BOC (Biological occurrence); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(nucleotide sequence; human G protein-coupled receptor 14926, its cDNA sequence, and its diagnostic and therapeutic uses)

IT 260242-64-6
RL: PRP (Properties)
(unclaimed protein sequence; human G protein-coupled receptor 14926, its cDNA sequence, and its diagnostic and therapeutic uses)

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Hillier; The WashU-Merck EST Project 1995
(2) Stadel, J; TRENDS IN PHARMACOLOGICAL SCIENCES, GB, ELSEVIER TRENDS JOURNAL V18(11), P430 CAPLUS
(3) Strausberg; Cancer Genome Anatomy Project 1998
(4) Synaptic Pharma Corp; EP 0787797 A 1997 CAPLUS

L17 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 4
AN 2000:850623 CAPLUS
DN 135:13785
TI Development of a ubiquitin transfer assay for high throughput screening by fluorescence resonance energy transfer

Epitopes
Genetic mapping
Immunoassay
Molecular cloning
Nucleic acid hybridization
Test kits
(human G protein-coupled receptor 14926, its cDNA sequence, and its diagnostic and therapeutic uses)

IT **Antibodies**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(human G protein-coupled receptor 14926, its cDNA sequence, and its diagnostic and therapeutic uses)

IT Gene, animal
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(mapping to chromosome 7; human G protein-coupled receptor 14926, its cDNA sequence, and its diagnostic and therapeutic uses)

IT Brain
Heart
Hyperplasia
Inflammation
Kidney
Liver
Lung
Muscle
Spleen
(modulation of receptor activity in; human G protein-coupled receptor 14926, its cDNA sequence, and its diagnostic and therapeutic uses)

IT Protein sequences
(of human G protein-coupled receptor 14926)

IT Animal
(transgenic; human G protein-coupled receptor 14926, its cDNA sequence, and its diagnostic and therapeutic uses)

IT 243132-22-1DP, subfragments are claimed
RL: BOC (Biological occurrence); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(amino acid sequence; human G protein-coupled receptor 14926, its cDNA sequence, and its diagnostic and therapeutic uses)

IT 260239-96-1P
RL: BOC (Biological occurrence); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(nucleotide sequence; human G protein-coupled receptor 14926, its cDNA sequence, and its diagnostic and therapeutic uses)

IT 260242-64-6
RL: PRP (Properties)
(unclaimed protein sequence; human G protein-coupled receptor 14926, its cDNA sequence, and its diagnostic and therapeutic uses)

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Hillier; The WashU-Merck EST Project 1995
(2) Stadel, J; TRENDS IN PHARMACOLOGICAL SCIENCES, GB, ELSEVIER TRENDS JOURNAL V18(11), P430 CAPLUS
(3) Strausberg; Cancer Genome Anatomy Project 1998
(4) Synaptic Pharma Corp; EP 0787797 A 1997 CAPLUS

L17 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 4
AN 2000:850623 CAPLUS
DN 135:13785
TI Development of a ubiquitin transfer assay for high throughput screening by fluorescence resonance energy transfer

AU Boisclair, Michael D.; McClure, Christopher; Josiah, Serene; Glass, Susan; Bottomley, Steve; Kamerkar, Shubi; Hemmila, Ilkka
CS GPC Biotech, Inc., Cambridge, MA, USA
SO Journal of Biomolecular Screening (2000), 5(5), 319-328
CODEN: JBISF3; ISSN: 1087-0571
PB Mary Ann Liebert, Inc.
DT Journal
LA English
CC 1-1 (Pharmacology)
AB An assay based on fluorescence resonance energy transfer (FRET) has been developed to screen for ubiquitination inhibitors. The assay measures the transfer of ubiquitin from Ubc4 to HECT protein Rsc 1083. Secondary reagents (streptavidin and **antibody** to glutathione-S-transferase [GST]), pre-labeled with fluorophores (europium chelate, Eu3+, and allophycocyanin [APC]), are noncovalently attached via tags (biotin and GST) to the reactants (ubiquitin and Rsc). When Rsc is ubiquitinated, Eu3+ and APC are brought into **close proximity**, permitting energy transfer between the two fluorescent labels. FRET was measured as time-resolved fluorescence at the emission wave-length of APC, almost entirely free of nonspecific fluorescence from Eu3+ and APC. The FRET assay generated a lower ratio of **signal** to background (8 vs. 31) than an assay for the same ubiquitination step that was developed as a dissocn.-enhanced lanthanide fluoroimmunoassay (DELFIA). However, compared to the DELFIA method, use of FRET resulted in higher precision (4% vs. 11% intraplate coeff. of variation). Quenching of fluorescence was minimal when compds. were screened at 10 .mu.g/mL using FRET. Employing a quick and simple homogeneous method, the FRET assay for ubiquitin transfer is ideally suited for high throughput screening.
ST ubiquitin transfer assay high throughput screening
IT Bioassay
(FRET; ubiquitin transfer assay for high throughput screening by fluorescence resonance energy transfer)
IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(HECT, Rsc 1083; ubiquitin transfer assay for high throughput screening by fluorescence resonance energy transfer)
IT Immunoassay
(fluorescence; ubiquitin transfer assay for high throughput screening by fluorescence resonance energy transfer)
IT **Drug** screening
(for ubiquitin inhibitors; ubiquitin transfer assay for high throughput screening by fluorescence resonance energy transfer)
IT Fluorometry
(ubiquitin transfer assay for high throughput screening by fluorescence resonance energy transfer)
IT 60267-61-0, Ubiquitin
RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(ubiquitin transfer assay for high throughput screening by fluorescence resonance energy transfer)
RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Earnshaw, D; J Biomol Screen 1999, V4, P239 CAPLUS
(2) Handley, P; Proc Natl Acad Sci USA 1991, V88, P258 CAPLUS
(3) Hemmila, I; Anal Biochem 1984, V137, P335 CAPLUS
(4) Hemmila, I; Drug Discov Today 1997, V2, P373 CAPLUS
(5) Hemmila, I; High Throughput Screening 1997, V2, P211
(6) Jentsch, S; Annu Rev Genet 1992, V26, P179 CAPLUS
(7) Jentsch, S; Cell 1995, V82, P881 CAPLUS
(8) Kolb, J; J Biomol Screen 1996, V1, P203 CAPLUS
(9) Mathis, G; Clin Chem 1993, V39, P1953 CAPLUS
(10) Mathis, G; Clin Chem 1995, V41, P1391 CAPLUS

AU Boisclair, Michael D.; McClure, Christopher; Josiah, Serene; Glass, Susan; Bottomley, Steve; Kamerkar, Shubi; Hemmila, Ilkka
CS GPC Biotech, Inc., Cambridge, MA, USA
SO Journal of Biomolecular Screening (2000), 5(5), 319-328
CODEN: JBISF3; ISSN: 1087-0571
PB Mary Ann Liebert, Inc.
DT Journal
LA English
CC 1-1 (Pharmacology)
AB An assay based on fluorescence resonance energy transfer (FRET) has been developed to screen for ubiquitination inhibitors. The assay measures the transfer of ubiquitin from Ubc4 to HECT protein Rsc 1083. Secondary reagents (streptavidin and **antibody** to glutathione-S-transferase [GST]), pre-labeled with fluorophores (europium chelate, Eu3+, and allophycocyanin [APC]), are noncovalently attached via tags (biotin and GST) to the reactants (ubiquitin and Rsc). When Rsc is ubiquitinated, Eu3+ and APC are brought into **close proximity**, permitting energy transfer between the two fluorescent labels. FRET was measured as time-resolved fluorescence at the emission wave-length of APC, almost entirely free of nonspecific fluorescence from Eu3+ and APC. The FRET assay generated a lower ratio of **signal** to background (8 vs. 31) than an assay for the same ubiquitination step that was developed as a dissocn.-enhanced lanthanide fluoroimmunoassay (DELFIA). However, compared to the DELFIA method, use of FRET resulted in higher precision (4% vs. 11% intraplate coeff. of variation). Quenching of fluorescence was minimal when compds. were screened at 10 .mu.g/mL using FRET. Employing a quick and simple homogeneous method, the FRET assay for ubiquitin transfer is ideally suited for high throughput screening.
ST ubiquitin transfer assay high throughput screening
IT Bioassay
(FRET; ubiquitin transfer assay for high throughput screening by fluorescence resonance energy transfer)
IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(HECT, Rsc 1083; ubiquitin transfer assay for high throughput screening by fluorescence resonance energy transfer)
IT Immunoassay
(fluorescence; ubiquitin transfer assay for high throughput screening by fluorescence resonance energy transfer)
IT **Drug** screening
(for ubiquitin inhibitors; ubiquitin transfer assay for high throughput screening by fluorescence resonance energy transfer)
IT Fluorometry
(ubiquitin transfer assay for high throughput screening by fluorescence resonance energy transfer)
IT 60267-61-0, Ubiquitin
RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(ubiquitin transfer assay for high throughput screening by fluorescence resonance energy transfer)
RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
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(1) Earnshaw, D; J Biomol Screen 1999, V4, P239 CAPLUS
(2) Handley, P; Proc Natl Acad Sci USA 1991, V88, P258 CAPLUS
(3) Hemmila, I; Anal Biochem 1984, V137, P335 CAPLUS
(4) Hemmila, I; Drug Discov Today 1997, V2, P373 CAPLUS
(5) Hemmila, I; High Throughput Screening 1997, V2, P211
(6) Jentsch, S; Annu Rev Genet 1992, V26, P179 CAPLUS
(7) Jentsch, S; Cell 1995, V82, P881 CAPLUS
(8) Kolb, J; J Biomol Screen 1996, V1, P203 CAPLUS
(9) Mathis, G; Clin Chem 1993, V39, P1953 CAPLUS
(10) Mathis, G; Clin Chem 1995, V41, P1391 CAPLUS

(11) Mellor, G; J Biomol Screen 1998, V3, P91 CAPLUS
(12) Morrison, L; Anal Biochem 1988, V174, P101 CAPLUS
(13) Rolfe, M; J Mol Med 1997, V75, P5 CAPLUS
(14) Rolfe, M; Proc Natl Acad Sci USA 1995, V92, P3264 CAPLUS
(15) Scheffner, M; Cell 1993, V75, P495 CAPLUS
(16) Selvin, P; J Am Chem Soc 1994, V116, P6029 CAPLUS
(17) Selvin, P; Methods Enzymol 1995, V246, P300 CAPLUS
(18) Selvin, P; Proc Natl Acad Sci USA 1994, V91, P10024 CAPLUS
(19) Stenroos, K; Cytokine 1998, V10, P495 CAPLUS
(20) Szllosi, J; Cytometry 1998, V34, P159
(21) Van Der Meer, B; Resonance Energy Transfer: Theory and Data 1994
(22) Wu, P; Anal Biochem 1994, V218, P1 CAPLUS
(23) Zhang, J; J Biomol Screen 1999, V4, P67

(11) Mellor, G; J Biomol Screen 1998, V3, P91 CAPLUS
(12) Morrison, L; Anal Biochem 1988, V174, P101 CAPLUS
(13) Rolfe, M; J Mol Med 1997, V75, P5 CAPLUS
(14) Rolfe, M; Proc Natl Acad Sci USA 1995, V92, P3264 CAPLUS
(15) Scheffner, M; Cell 1993, V75, P495 CAPLUS
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(17) Selvin, P; Methods Enzymol 1995, V246, P300 CAPLUS
(18) Selvin, P; Proc Natl Acad Sci USA 1994, V91, P10024 CAPLUS
(19) Stenroos, K; Cytokine 1998, V10, P495 CAPLUS
(20) Szllosi, J; Cytometry 1998, V34, P159
(21) Van Der Meer, B; Resonance Energy Transfer: Theory and Data 1994
(22) Wu, P; Anal Biochem 1994, V218, P1 CAPLUS
(23) Zhang, J; J Biomol Screen 1999, V4, P67

L13 ANSWER 8 OF 8 MEDLINE
AN 94197071 MEDLINE
DN 94197071 PubMed ID: 8147276
TI Use of drug-specific **antibodies** to identify ethidium adducts produced in Trypanosoma brucei by photoaffinity labeling.
AU Omholt P E; Cox B A; Prine L C; Byrd S; Yielding L W; Yielding K L
CS Department of Human Biological Chemistry and Genetics, University of Texas Medical Branch, Galveston 77550.
NC AI17700 (NIAID)
SO ACTA TROPICA, (1993 Dec) 55 (4) 191-204.
Journal code: 0370374. ISSN: 0001-706X.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199405
ED Entered STN: 19940511
Last Updated on STN: 19940511
Entered Medline: 19940504
AB A photoreactive azido analog of the trypanocide ethidium bromide, 3-amino-8-azido-5-ethyl-6-phenylphenanthridinium chloride, attached covalently to calf thymus DNA (CT DNA) by photoaffinity labeling, was used to generate **antibodies** for the **drug analog**.
The specificity of the antiserum was tested using **enzyme**-linked immunoadsorbant assays (ELISA) against immobilized antigen (photoaffinity labeled DNA) and by both the avidin-biotin peroxidase reaction and indirect immunofluorescence performed on smears of drug treated trypanosomes. The reaction of the antiserum with the covalently bound drug adduct was diminished effectively by prior incubation with an excess of ethidium monoazide, ethidium diazide, and ethidium bromide, and to a lesser extent by the DNA-ethidium complex, the diazide-DNA or RNA adduct, and the monoazide-RNA adduct. DNA which had been photoaffinity labeled with either the propidium or the acridine moiety did not react. The antiserum recognition of DNA photoaffinity labeled with ethidium monoazide was based on the substituted phenanthridinium ring system of the parent ethidium, as evidenced by competition binding studies involving the free monoazido analog (EA1), the diazido analog (EA2), and the parent compound, ethidium bromide (EB). This approach and the sensitivity it provides should prove useful for identifying the distribution and fate of covalently bound drugs resulting from antiparasitic drug treatment, and for studying their roles in antiparasitic action.
CT Check Tags: Animal; Support, U.S. Gov't, P.H.S.
Affinity Labels
Antibodies
Antibody Specificity
Cattle
*DNA: ME, metabolism
Enzyme-Linked Immunosorbent Assay: MT, methods
Ethidium: IM, immunology
*Ethidium: ME, metabolism
Fluorescent Antibody Technique
Immunoenzyme Techniques
Sensitivity and Specificity
*Trypanosoma brucei brucei: ME, metabolism
RN 3546-21-2 (Ethidium); 9007-49-2 (DNA)
CN 0 (Affinity Labels); 0 (**Antibodies**)

=>

L4 ANSWER 8 OF 21 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2
AN 1993:322462 BIOSIS
DN PREV199396030812
TI **Simultaneous** incorporations of two anticancer **drugs** into DNA: The structures of formaldehyde cross-linked adducts of daunorubicin-d(CG(araC)GCG) and doxorubicin-d(CA(araC)GTG) complexes at high resolution.
AU Zhang, Hong; Gao, Yi-Gui; Van Der Marel, Gijs A.; Van Boom, Jacques H.; Wang, Andrew H.-J. (1)
CS (1) Div. Biophys., Dep. Cell Struct. Biol., Univ. Ill. Urbana-Champaign, Urbana, IL 61801 USA
SO Journal of Biological Chemistry, (1993) Vol. 268, No. 14, pp. 10095-10101. ISSN: 0021-9258.
DT Article
LA English
AB Anthracycline antibiotics (notably daunorubicin (DAU) and doxorubicin (DOX)) and nucleoside analog arabinosylcytosine (araC or aC) are important anticancer **drugs**. They are sometimes used together in the treatment of certain cancers. Both classes of compounds act by blocking DNA replication and transcription. To probe whether both **drugs** can be incorporated simultaneously into DNA and the possible structural consequences, we carried out x-ray diffraction analyses of the complexes between DAU/DOX and araCcontaining DNA hexamers cross-linked with formaldehyde. The crystal structures were determined to high resolution (DAU-CG-aCGCG, 1.2 ANG , space group P4-12-12, R = 0.182, 3275 reflections; DOX-CA-aCGTG, 1.5 ANG , space group C2, R = 0.175, 3359 reflections), and they are similar to those of the previously studied DAU- and DOX-DNA complexes, despite different crystal packings. Two DAU/DOX molecules intercalate at both ends of the helix with their amino sugars in the minor groove. As in the structure of DAU-CGCGCG (Wang, A. H.-J., Gao, Y.-G., Liaw, Y.-C., and Li, Y. K. (1991) Biochemistry 30, 3812-3815), a covalent methylene bridge (from formaldehyde) between the N-3' of daunosamine and the N-2 of the guanine is formed in both adducts. In DOX-CA-aCGTG, the two halves are slightly different with a root-mean-square deviation of 0.322 ANG between them. The O-14 hydroxyls of the intercalated DOXs are within hydrogen bond distances to the O-2P atoms of the A2p(aC3) and A8p(aC9) steps. The O-2'-hydroxyl group from araC does not affect the binding of DAU-DOX or the conformation of the **drug**-DNA complexes. The results suggest that three major **drug** modifications on DNA, i.e., intercalation, covalent bond formation, and nucleoside analog incorporation, can coexist in the same DNA molecule without difficulty. When they occur in **close proximity** in DNA, they may provide an additive inhibitory effect for the target enzymes.
CC Biochemical Studies - General *10060
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies - Carbohydrates *10068
Biophysics - Molecular Properties and Macromolecules *10506
Pharmacology - General *22002
Neoplasms and Neoplastic Agents - Therapeutic Agents; Therapy *24008
IT Major Concepts
Biochemistry and Molecular Biophysics; Pharmacology; Tumor Biology
IT Chemicals & Biochemicals
FORMALDEHYDE; DAUNORUBICIN; DOXORUBICIN
IT Miscellaneous Descriptors
CLONOGENIC FRACTION; INTERCELLULAR COMMUNICATION; OXYGENATION; STEM CELLS
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates

L4 ANSWER 8 OF 21 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2

AN 1993:322462 BIOSIS

DN PREV199396030812

TI **Simultaneous** incorporations of two anticancer **drugs** into DNA: The structures of formaldehyde cross-linked adducts of daunorubicin-d(CG(araC)GCG) and doxorubicin-d(CA(araC)GTG) complexes at high resolution.

AU Zhang, Hong; Gao, Yi-Gui; Van Der Marel, Gijs A.; Van Boom, Jacques H.; Wang, Andrew H.-J. (1)

CS (1) Div. Biophys., Dep. Cell Struct. Biol., Univ. Ill. Urbana-Champaign, Urbana, IL 61801 USA

SO Journal of Biological Chemistry, (1993) Vol. 268, No. 14, pp. 10095-10101. ISSN: 0021-9258.

✓ pulled. (A)

DT Article

LA English

AB Anthracycline antibiotics (notably daunorubicin (DAU) and doxorubicin (DOX)) and nucleoside analog arabinosylcytosine (araC or aC) are important anticancer **drugs**. They are sometimes used together in the treatment of certain cancers. Both classes of compounds act by blocking DNA replication and transcription. To probe whether both **drugs** can be incorporated simultaneously into DNA and the possible structural consequences, we carried out x-ray diffraction analyses of the complexes between DAU/DOX and araCcontaining DNA hexamers cross-linked with formaldehyde. The crystal structures were determined to high resolution (DAU-CG-aCGCG, 1.2 ANG , space group P4-12-12, R = 0.182, 3275 reflections; DOX-CA-aCGTG, 1.5 ANG , space group C2, R = 0.175, 3359 reflections), and they are similar to those of the previously studied DAU- and DOX-DNA complexes, despite different crystal packings. Two DAU/DOX molecules intercalate at both ends of the helix with their amino sugars in the minor groove. As in the structure of DAU-CGCGCG (Wang, A. H.-J., Gao, Y.-G., Liaw, Y.-C., and Li, Y. K. (1991) Biochemistry 30, 3812-3815), a covalent methylene bridge (from formaldehyde) between the N-3' of daunosamine and the N-2 of the guanine is formed in both adducts. In DOX-CA-aCGTG, the two halves are slightly different with a root-mean-square deviation of 0.322 ANG between them. The O-14 hydroxyls of the intercalated DOXs are within hydrogen bond distances to the O-2P atoms of the A2p(aC3) and A8p(aC9) steps. The O-2'-hydroxyl group from araC does not affect the binding of DAU-DOX or the conformation of the **drug**-DNA complexes. The results suggest that three major **drug** modifications on DNA, i.e., intercalation, covalent bond formation, and nucleoside analog incorporation, can coexist in the same DNA molecule without difficulty. When they occur in **close proximity** in DNA, they may provide an additive inhibitory effect for the target enzymes.

CC Biochemical Studies - General *10060
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies - Carbohydrates *10068
Biophysics - Molecular Properties and Macromolecules *10506
Pharmacology - General *22002
Neoplasms and Neoplastic Agents - Therapeutic Agents; Therapy *24008

IT Major Concepts
Biochemistry and Molecular Biophysics; Pharmacology; Tumor Biology

IT Chemicals & Biochemicals
FORMALDEHYDE; DAUNORUBICIN; DOXORUBICIN

IT Miscellaneous Descriptors
CLONOGENIC FRACTION; INTERCELLULAR COMMUNICATION; OXYGENATION; STEM CELLS

ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
human (Hominidae)

ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates

RN 50-00-0 (FORMALDEHYDE)
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23214-92-8 (DOXORUBICIN)

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